REMARKS

Previously Claims 1-12 were pending. In the instant amendments, Claims 3, 4 and 8 have been canceled. Claims 1, 5, 6, 9 and 11 have been amended. New Claims 21-25 have been added. Upon entry of the amendments, Claims 1, 2, 5-7, 9-12 and 21-25 will be pending and under consideration.

I. AMENDMENTS TO THE CLAIMS

Claims 3, 4 and 8 have been canceled.

The amendment to Claim 1 is supported, for example, by the specification at page 1, lines 21-26; page 2, lines 25-35; page 4, lines 19-21; page 9, lines 9-10; page 12, lines 11-18; page 13, lines 22-26; and page 14, lines 14-22.

Claims 5 and 9 have been amended in their dependencies.

Claim 6 has been amended to recite, in pertinent part, a solid substrate on which the coding oligonucleotide is immobilized. Support for this amendment is found in the specification, for example, at page 7, lines 28-29; page 8, lines 28-29; page 9, lines 23-35; and page 10, lines 1-29.

Claim 11 has been amended to recite, in pertinent part, "and the first polynucleotide and the second polynucleotide are each independently linked to the solid substrate." Support for this amendment is found in specification, for example, at page 9, lines 24, to page 10, line 24, and Figure 1B.

New Claim 21 is supported, for example, by the specification at page 8, lines 1-4 and page 9, lines 13-15.

New Claim 22 is supported, for example, by the specification at page 9, lines 16-22.

New Claim 23 is supported, for example, by the specification at page 10, lines 25-29, and Figure 1C.

New Claim 24 is supported, for example, by the specification at page 2, lines 25-28; page 7, line 21; page 13, lines 5-7; and page 14, lines 20-21.

Support for new Claim 25 is found in the specification, for example, at page 9, lines 23-35 and in Figure 1B.

No new matter has been added by the amendments. As the amendments are fully supported by the specification and claims as filed, entry of the amendments is respectfully requested.

No amendment fee is believed to be due since both the total number of claims and the number of independent claims after entry of the amendments are fewer than those previously paid for by Applicants.

II. CLAIM REJECTION UNDER 35 U.S.C. § 112, SECOND PARAGRAPH

Claims 1-12 stand rejected under 35 U.S.C. § 112, second paragraph, allegedly as being indefinite. Specifically, the Examiner alleges that it is unclear how Claims 3 and 4 further define Claim 1, thereby rendering unclear what type of structure would be a "coded test unit" in Claim 1. Claims 2 and 5-12 are included in the rejection as being dependent from Claim 1, 3 or 4. Applicants respectfully submit that the rejection is obviated in view of the amendment to Claim 1 and the cancellation of Claims 3 and 4. Accordingly, it is respectfully requested that the rejection of Claims 1-12 under 35 U.S.C. § 112, second paragraph, be withdrawn.

Claim 6 stands rejected under 35 U.S.C. § 112, second paragraph, as indefinite, allegedly since it is unclear how a coded test unit can comprise a solid support. Applicants respectfully traverse.

Amended Claim 6 recites that the coded test unit further comprises a solid substrate on which the coding oligonucleotide is immobilized. The Patent Office contends that Claim 6 is unclear regarding whether the coded test unit comprises the solid support and a bound oligonucleotide or if the oligonucleotides surround, are linked to, or are surrounded by a substrate. As provided in the specification, *if* a coded test unit comprises a solid substrate there must be some means of associating the coding oligonucleotide and test moiety with the solid substrate such as by, for example, non-covalent adsorption or by covalent linkages (*see, e.g.,* page 9, lines 27-35), regardless of whether the coding oligonucleotide and test moiety are surrounded by the solid substrate (*e.g.*, in a porous substrate) or surround the solid substrate (*e.g.*, on a non-porous substrate). Applicants respectfully submit Claim 6 recites such a feature, *i.e.*, "a solid substrate on which the coding oligonucleotide is immobilized."

Applicants respectfully submit that Claim 6 meets the patentability requirements of 35 U.S.C. § 112, second paragraph, and respectfully request the withdrawal of the rejection of Claim 6 under 35 U.S.C. § 112, second paragraph.

III. CLAIM REJECTION UNDER 35 U.S.C. § 102(b) OVER BENNER *et al.*

Claims 1-12 stand rejected under 35 U.S.C. § 102(b), allegedly as being anticipated by Benner (U.S. Patent No. 5,432,272; "Benner"). The rejection of Claims 3, 4 and 8 is moot

in view of the cancellation of these claims. Applicants respectfully traverse the rejection of claims 1, 2, 5-7 and 9-12.

A single prior art reference anticipates a patent claim if it expressly or inherently describes each and every limitation set forth in the patent claim. *Trintec Indus., Inc. v. Top-U.S.A. Corp.*, 295 F.3d 1292, 1295, 63 U.S.P.Q.2d 1597, 1599 (Fed. Cir. 2002). Applicant respectfully submits that Benner does not teach each and every limitation of any rejected claim.

Amended Claim 1 recites, in pertinent parts, a method of identifying a coded test unit *in a plurality* of coded test units, comprising *contacting the plurality* of coded test units with a decoding oligonucleotide under conditions in which the decoding oligonucleotide produces a detectable hybridization signal *sufficient to distinguish* the coded test unit from the remainder of the plurality of coded test units whereby the coded test unit is identified. Benner teaches that a single primer in a reaction can be extended to incorporate a non-standard base, and Benner exemplifies this using two different primers, the 8-mer and 18-mer primers that are depicted in Figure 5 of Benner. Benner does not teach or suggest all the elements recited in the method of instant Claim 1.

For example, Benner teaches a method of synthesizing oligonucleotides from template strands containing a non-standard base, either 3β-D-ribofuranosyl-2,6-diaminopyrimidine ("K") or "iso-C." Although seven pairs of oligonucleotide strands (*i.e.*, primer + template strands) are shown in Figure 5 of Benner, it is clear from the text accompanying the examples that Benner does not teach using these pairs of oligonucleotides in the method recited in instant Claim 1.

To illustrate, Benner describes T7 RNA polymerase reactions in which only a *single type* of 18-mer primer with a *single type* of K-containing template and upon completion of the reaction all of the individual 18-mer primers are extended to incorporate a xanthosine triphosphate ("X") opposite the K in the template strand. *See* column 7, lines 1-12, and 56-68. The Patent Office suggests that the 18-mer can be viewed as a "coded test unit" as recited in Claim 1, and the K-containing template as the "decoding oligonucleotide." However, Benner does not teach or suggest contacting a plurality of coded test units with the decoding oligonucleotide as recited in instant Claim 1. In Benner, there is no coded test unit *in a plurality of coded test units*. Even if the individual 18-mer molecules are considered as a "plurality," then because all the individual 18-mer molecules are identical no "coded test unit" can be identified from the plurality of coded test units in these reactions as recited in Claim 1. Nor does the K-containing template in Benner, if viewed as a "decoding

oligonucleotide," produce a detectable hybridization signal *sufficient to distinguish* any coded test unit from the remainder of the plurality of coded test units as recited in Claim 1, since the extension of the primers is presumably the same for all of the 18-mer primers. (The extension of the primer would have to be the "coding oligonucleotide" since only this part of the primer comprises a orthogonal nucleobase that could be *complementary* to the decoding oligonucleotide as recited in Claim 1).

Not one of the other reactions described in Benner can be understood to be teaching the method of instant Claim 1. For example, reactions using DNA polymerase I are described using a particular "K"-containing template plus a 8-mer primer. *See* column 8, lines 1-15. No plurality of coded test units are taught or suggested by Benner. Benner describes other sets of reactions in which only an iso-C-containing template is used with a single type of primer per reaction. *See, e.g.*, column 9, lines 3-20 (describing reactions with an iso-C-containing template plus 8-mer primer using DNA polymerase I), and column 10, lines 15-21 (describing reactions with another iso-C-containing template plus 18-mer primer using T7 RNA polymerase). Again, Benner does not teach or suggest a plurality of coded test units, or contacting a plurality of coded test units, and therefore Benner does not teach or suggest the method of Claim 1 of identifying a coded test unit in a plurality of coded test units.

Furthermore, amended Claim 1 is a method directed towards *identification* of a coded test unit in a plurality of coded test units. Benner does not teach *identification* of a coded test unit because all of the components of the reaction described by Benner are known. The common, ordinary meaning of "identify" is "1. [t]o establish the identity of." American Heritage College Dictionary, Third Edition, Houghton Mifflin Co., Boston (1997), at page 674. The extension taught by Benner does not "establish the identity of" any of the reaction components. Indeed, the primers that the Patent Office contends may be viewed as the "test moieties" cannot be varied in these reactions since doing so prevents extension and formation of a "coded test unit." Thus, the method of Benner does not "identify" a coded test unit from a plurality of coded test units.

For the above reasons, Applicants respectfully submit that Benner does not anticipate Claim 1 or any of Claims 2, 5-7 and 9-12 that depend from Claim 1.

With regard to Claim 2, not only does Benner fail to teach each and every element of the base Claim 1 from which Claim 2 depends, but Claim 2 requires that a second molecule in the plurality of coded test units be identified. Even assuming that the 8-mer or 18-mer can be viewed as being "identified" by its extension, Benner does not teach using the same

plurality to identify a *second* molecule, as recited in the second step of Claim 2. For this reason, Benner does not teach or suggest every limitation in Claim 2.

With regard to Claim 6, the Patent Office alleges that the vessel containing the reactions described in Benner can be viewed as a "solid substrate." Applicants respectfully disagree. As explained above, the specification teaches that if a coded test unit comprises a solid substrate, for example, as recited in Claim 6, then the coding oligonucleotide of the coded test unit is immobilized, either directly or indirectly, to the solid substrate. *See, e.g.*, page 7, lines 28-29, and page 9, line 23, to page 10, line 29. To the extent that the primers used in Benner can be viewed as coded test units, nothing in Benner teaches any particular association between the primers and the reaction vessels, and therefore, Benner does not teach or suggest a coded test unit comprising a solid substrate with which the coding oligonucleotide is immobilized. Accordingly, Applicants respectfully submit that Benner does not anticipate Claim 6 or any of Claims 7 and 9-12 that depend from Claim 6.

The Patent Office suggests that, with regard to claim 7, the 8-mer and 18-mer primers described in Benner can be considered as a first substrate and a second substrate. Office Action at page 7. Applicants respectfully submit that the specification at page 7, lines 28-29, clearly defines a substrate as any solid support capable of having a coding oligonucleotide or test moiety immobilized thereon. Applicants respectfully submit that a 8-mer or 18-mer nucleic acid is not normally considered to constitute a solid support. The examples of substrates provided on page 10, lines 3-8, further indicates that, as taught by the instant specification, those of skill in the art would not consider the 8-mer and 18-mer primers described in Benner to be a substrate.

The Patent Office contends that, with regard to Claim 7, nothing requires that the coded substrates are contained within the same mixture. However, Claim 7 recites that the first and second substrates be identified *in the plurality* of coded substrates. Moreover, Claim 7, being dependent from Claim 6, requires that the coded oligonucleotide be immobilized on the substrate. Benner does not teach or suggest this since there is no particular association between the primers used in the reactions described in Benner and the reaction vessels used in those reactions. Accordingly, Applicants respectfully submit that Benner does not teach or suggest each and every limitation of Claim 7.

With regard to Claim 11, Benner does not teach or suggest any oligonucleotide to be immobilized to a solid substrate, much less having a first polynucleotide and a second polynucleotide each independently linked to a solid substrate. Accordingly, Applicants

respectfully submit that Benner does not teach or suggest each and every limitation of Claim 11.

In sum, Applicants respectfully submit that Benner does not teach or suggest each and every limitation set forth in any of Claims 1, 2, 5-7, and 9-12.

For the above reasons, Applicants respectfully request that the rejection of Claims 1-12 under 35 U.S.C. § 102(b) be withdrawn.

With regard to new Claims 21-25, not only does Benner fail to teach each and every element of the base Claim 1 from which the new claims depend, but in addition Benner fails to teach or suggest all the limitations of these new claims. In particular, Benner does not teach or suggest a polypeptide as recited in new Claim 21, nor does Benner teach or suggest immobilization of any possible coded test unit or test moiety or coding oligonucleotide thereof, upon a solid substrate, for example, as recited in Claims 23 and 25. Accordingly, Applicants respectfully submit that new Claims 21-24 are patentable under 35 U.S.C. § 102(b).

IV. CLAIM REJECTION UNDER 35 U.S.C. § 102(b) OVER COLLINS *et al.*

Claims 1-12 stand rejected under 35 U.S.C. § 102(b), allegedly as being anticipated by Collins (U.S. Patent No. 5,681,702) ("Collins"). The rejection of Claims 3, 4 and 8 is moot in view of the cancellation of these claims. Applicants respectfully traverse the rejection of Claims 1, 2, 5-7 and 9-12, since Collins does not teach each and every limitation set forth in these claims. *See Trintec Indus., Inc. v. Top-U.S.A. Corp.*, 295 F.3d 1292, 1295, 63 U.S.P.Q.2d 1597, 1599 (Fed. Cir. 2002).

Collins discloses a nucleic acid detection assay for detecting a nucleic acid analyte (target) using a set of successively hybridizing nucleic acids (including the target) or "sandwich assay," wherein assay components that do not hybridize to the target comprise orthogonal nucleobases (termed universal sequences in Collins). Figure 1 of Collins depicts the assimilation of various nucleic acids into a structure that is formed in the detection assay. In particular, Figure 1 illustrates a capture probe ("CP") linked to a solid support having a nucleic acid sequence ("C-3") containing orthogonal nucleobases (indicated in Figure 1 by the heavy lines). C-3 hybridizes to a capture extender ("CE") at its "C-2" sequence, and the CE in turn hybridizes to the target via a different sequence having standard nucleobases. The target is detected by its hybridization via standard nucleobases to a label extender ("LE"). LE in turn hybridizes via optional orthogonal nucleobases in its "L-2" sequence to an amplifier at the amplifier's "M-1" sequence. A different site (identified as "M-2" in Figure 1) in the

amplifier in turn hybridizes via orthogonal nucleobases to the "L-3" sequence of a labeled probe ("LP").

Instant Claim 1 recites the use of a decoding oligonucleotide comprising an orthogonal nucleobase wherein the decoding oligonucleotide is complementary to the coding oligonucleotide of the coded test unit. The Patent Office identifies Collins' LP as the decoding oligonucleotide. The Patent Office alleges that the complex of solid support, CP, CE, target, LE, and optionally, amplifier, is the coded test unit.

Collins discloses assay components that, at first glance, appear to resemble components of the instantly claimed method. However the *method* disclosed by Collins differs significantly from the *method* of Claim 1. Claim 1 recites that the coded test unit identified comprises a test moiety and a coding oligonucleotide that enables one to distinguish the coded test unit from the remainder of the plurality of coded test units. This feature of having a coding oligonucleotide in a coded test unit that can be identified by distinguishing it in the contacting step from a plurality of coded test units is not taught or suggested by Collins since, at a minimum, Collins does not teach a *plurality of coded test units*.

With regard to the term plurality, as noted by the Patent Office, Collins states that in the sandwich assay, a plurality of capture probes are affixed to a solid surface. (*See* col. 12, lines 32-34). However, the method described in Collins "addresses the problem of hybridization-dependent assay background noise" (col. 23, lines 57-58), and the plurality of capture probes are present in order to increase binding of the analyte over the available surface area of the support without having to use natural DNA from, e.g., salmon sperm or calf thymus. *See* col. 12, lines 34-42; col. 15, lines 26-29. The conclusion to be drawn is that the plurality of capture probes are all directed towards the same analyte (or target). This is further supported by the fact that throughout the specification Collins explains that the analyte (used in the singular) will be bound by the capture probes (plural). For example, "...an assay is provided in which the melt temperature...of the complex formed between the analyte and the support-bound capture probes..." (*see* col. column 4, lines 58-60); "This complex may be subsequently added . . . to a solid phase having the capture probes bound to the surface thereof" (*see* col. column 9, lines 59-62); "The stringency is altered . . . which thereby affords the physical separation of the target molecule from the capture probes" (*see* col. column 9, lines 59-62). The kit claim 8 in Collins also recites that the plurality (or "set" as used in the claim) of capture probes and set of capture extenders bind to the analyte at "predetermined segments" of the analyte. Thus, Collins teaches that pluralities of capture

probes are used to increase specificity for a single analyte, or in other words, all the capture probes are directed towards capturing the same analyte. Collins does not teach or suggest a method of identifying a coded test unit in a plurality of coded test units.

Furthermore, Collins does not teach or suggest a coded test unit that can be distinguished from the remainder of the plurality of coded test units when contacted by the decoding oligonucleotide, as recited in instant Claim 1. Although the Patent Office identifies Collins' LP as the decoding oligonucleotide, nowhere does Collins teach or suggest use of the LP to distinguish a coded test unit from a plurality of coded test units. Again, Collins' describes a method to amplify a signal generated from a single analyte over background noise which can be assumed to not include a coded test unit. Nor does Collins' LP distinguish between the analyte bound to one capture probe versus the analyte bound to another of the "plurality of capture probes." Accordingly, Collins does not teach or suggest a method of identifying a coded test unit as recited in Claim 1.

For the above reasons, Applicants respectfully submit that Collins does not teach or suggest each and every limitation of Claim 1, or of Claims 2, 5-7, 9-12 and 21-24 that depend from Claim 1.

With regard to Claim 2, two steps are recited in the method. In addition to the fact that Collins does not teach or suggest a plurality of coded test units as explained above, nowhere does Collins teach or suggest a method in which a first molecule is identified in the plurality and then a second molecule is identified. In the methods described in Collins, any detection of the target using LP (which the Patent Office alleges to be the decoding oligonucleotide) means that capture probe is present on the solid substrate and that the target is present to allow a complex to form. But Collins does not teach or suggest coding to distinguish one complex from another using LP. Applicants respectfully submit that Collins does not teach or suggest each and every limitation of Claim 2 that recites a method for decoding a plurality of coded test units wherein a first molecule is identified and a second molecule is identified.

Claim 11 recites a method wherein a first polynucleotide comprises the test moiety and a second polynucleotide comprises the coding oligonucleotide and the first polynucleotide and the second polynucleotide are each independently linked to the solid substrate. Collins does not teach or suggest linking the coding oligonucleotide (*i.e.*, any of the universal sequences in Collins) to the solid substrate *independently* of the link of the test moiety (*i.e.*, the target in Collins) to the solid substrate. For these reasons, Applicants

respectfully submit that Collins does not teach or suggest each and every limitation of Claim 11.

In sum, Applicants respectfully submit that Collins does not teach or suggest each and every limitation set forth in any of Claims 1, 2, 5-7, and 9-12.

For the above reasons, Applicants respectfully request that the rejection of Claims 1-12 under 35 U.S.C. § 102(b) be withdrawn.

With regard to new Claims 21-25, not only does Collins fail to teach each and every element of the base Claim 1 from which the new claims depend, but in addition Collins fails to teach or suggest all the limitations of these new claims. For example, Collins does not teach or suggest a polypeptide as recited in new Claim 21, nor does Collins teach or suggest a method wherein the test moiety and the coding oligonucleotide are each independently covalently linked to the solid substrate. Accordingly, Applicants respectfully submit that new Claims 21-24 are patentable under 35 U.S.C. § 102(b).

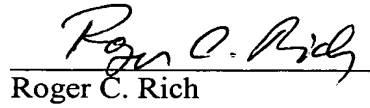
CONCLUSION

Applicant submits that the claims as presently pending meet all of the criteria for patentability and are in condition for allowance. Early notification to this effect is earnestly solicited. The Examiner is invited to call the undersigned attorney if a telephone call could help resolve any remaining items.

No fees, other than that for a Petition for Extension of Time, are believed due with this response. However, the Commissioner is authorized to charge any fees under 37 C.F.R. § 1.17, any underpayment of fees, or credit any overpayment Jones Day Deposit Account No. 503013 (order no. 9584-030-999) that may be required by this Amendment and Response.

Respectfully submitted,

Date: September 10, 2004



54,398

Roger C. Rich (Reg. No.)

For: Samuel B. Abrams (Reg. No. 30,605)

JONES DAY
222 East 41st Street
New York, New York 10017-6702
(212) 326-3939